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WESTERN DISTRICT OF LOUISIANA  
LAFAYETTE, LOUISIANA

UNITED STATES DISTRICT COURT  
WESTERN DISTRICT OF LOUISIANA  
LAFAYETTE DIVISION

IN RE: ACTOS® (PIOGLITAZONE)  
PRODUCTS LIABILITY LITIGATION

MDL No. 6:11-md-2299

JUDGE DOHERTY

This Document Applies To:  
*Allen, et. al. v. Takeda Pharmaceuticals  
North America, Inc., et al.*  
(Case No. 12-cv-00064)

MAGISTRATE JUDGE HANNA

**MEMORANDUM RULING:**  
**DAVID A. KESSLER, M.D.**

This multidistrict litigation arises from product liability claims against the manufacturer and marketer of Actos® and other drugs containing pioglitazone. Pending before this Court is the Defendants' Motion to Exclude Testimony of Plaintiffs' Expert, David A. Kessler, M.D.<sup>1</sup> For the following reasons, the Defendants' Motion will be DENIED IN PART AND GRANTED IN PART.

**EVIDENCE AT ISSUE**

David A. Kessler is a medical doctor, who works as a Professor of Pediatrics, Epidemiology and Biostatistics at the University of California, San Francisco. He served as the Commissioner of the United States Food and Drug Administration ("FDA") from 1990 to 1997, and currently serves as the Chair of compliance committees in two companies regulated by the FDA. He will be proffered as an expert in the areas of:

- regulatory compliance;

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<sup>1</sup> Rec. Doc. 3471. This motion has been urged on behalf of all named defendants in this matter. For these purposes only, the Court will not distinguish among the Defendants as there is no legal significance as to the Defendants as to this motion. The Memorandum in Support of Defendants' Motion to Exclude Testimony of Plaintiffs' Expert David Kessler, M.D. is found at Rec. Doc. 3471-1 ["Memorandum"]; the Plaintiffs' Memorandum of Law in Opposition to Defendants' Motion to Exclude Testimony of Plaintiffs' Expert David Kessler, M.D. is found at Rec. Doc. 3610-2 ["Opposition"]; and the Defendants' Reply in Support of Defendants' Motion to Exclude Testimony of Plaintiffs' Expert David Kessler, M.D. is found at Rec. Doc. 3671 ["Reply"].

- regulatory warnings;
- product labeling; and
- the standards of care for the manufacture and marketing/sale of pharmaceuticals.

Dr. Kessler's opinions are found throughout his Report. He has submitted a 161-page, 458-paragraph report,<sup>2</sup> together with four attached appendices (his curriculum vitae, a list of his prior testimony as an expert, a list of published articles about the FDA that he either authored or co-authored, and a 48-page list of the case materials that he has reviewed) and 28 schedules of information.

Dr. Kessler has not provided a definitive *list* of all of the opinions he developed in this case, but did include the following list summarizing his conclusions:

- In light of FDA's limited resources and scope, the purveyor of a drug, not the FDA, has primary responsibility for the safety of its product.
- Takeda omitted important information of a signal of disproportionate reporting of bladder cancer in its submissions to FDA.
- Takeda did not disclose that the clinical data as of January 2004 showed an increased risk of bladder cancer with ACTOS. This data should have resulted in disclosure to FDA and an adequate Warning to healthcare providers and patients. Based on my experience, such disclosures would have been important and necessary to FDA, healthcare providers and patients.
- As early as 1996, pre-clinical data revealed a signal of an increased risk of bladder cancer. Based on my experience, these data were reason for Takeda to closely scrutinize their clinical data for any clinical safety signal regarding bladder cancer risk.
- With the data from randomized, controlled clinical trials demonstrating a statistically significant increase in bladder cancer risk as of January 2004, Takeda had an obligation to add such information to the Warnings section of the ACTOS label.

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<sup>2</sup> "The Kessler Report," without its attached schedules, was submitted by the Plaintiffs as Exhibit 2 to the Opposition, and was submitted by the Defendants as Omnibus Exhibit C5. "The Kessler Deposition" was submitted by the Defendants as Omnibus Exhibit B5.

- In the face of scientific uncertainty regarding the similarities and differences in PPAR activity between ACTOS and dual PPAR agonists and the mechanism of urinary tumor formation, a reasonable and prudent pharmaceutical manufacturer would have agreed with FDA's position as early as 2002 to warn about increased bladder tumors.
- Between 2004 and 2011, Takeda did not provide an adequate warning of the increased risk of bladder cancer with ACTOS.
- Takeda's Company Core Data Sheet included information about the increased risk of bladder cancer and ACTOS based on pre-clinical data and a meta-analysis of clinical and epidemiological study data. The data that was necessary to make this conclusion was available to Takeda on January 2004. This further reinforces the fact that Takeda was in a position to make the Warning regarding bladder cancer and ACTOS earlier and that such Warning was important and necessary.
- Data from the KPNC study second interim analysis demonstrated an increased risk of bladder cancer with ACTOS exposure for 12-24 months and > 24 months, which should have been included in Warnings to physicians and patients, years before the data from the third interim analysis appeared in the August 2011 actos [sic] label.
- In 2011, Takeda's Warning about bladder cancer was inadequate because it omitted important data from a meta-analysis of Takeda's randomized clinical trials.
- Since 2011, Takeda's sales force communications and speakers' presentations were misleading, because they omitted important data from the meta-analysis of Takeda's randomized clinical trials.
- Takeda had a responsibility to assure that significant safety risks were not minimized, instead of explaining away the bladder cancer risk.
- The lack of an adequate Warning about the increased risk of bladder cancer is demonstrated by the fact that the professional medical society diabetic guidelines make no mention of the increased bladder risk until after July 2011.
- Takeda's promotion of ACTOS was misleading.
- Takeda's and Lilly's promotion of ACTOS' cardiovascular benefits from 2001 to 2005 was misleading.
- Takeda's promotion of ACTOS' cardiovascular benefits since 2005 was misleading.

- Takeda's promotion of ACTOS for cardiovascular benefits to physicians and patients for [*sic*] since 2005 was improper.
- To FDA, Takeda implied no clinical significance of ACTOS' PPAR-alpha activity. In sales force communications and materials, they implied a clinical significance of ACTOS' PPAR-alpha activity. Takeda selectively presented the science to support the position the company wanted to promote.<sup>3</sup>

Regrettably, while the current motion was filed on the deadline for Daubert motions in limine, the arguments made by Defendants conflate true Daubert challenges with the more general *limine*-type challenges creating an analytical challenge. Consequently, each of the Defendants' challenges or arguments will be addressed separately with an eye to the somewhat different evidentiary issues existing.

#### APPLICABLE LAW

While state law governs the Plaintiffs' claims in this matter, the Federal Rules of Evidence control the admission of expert testimony.<sup>4</sup> Under the Federal Rules of Evidence, "relevant" evidence is admissible, while irrelevant evidence not admissible.<sup>5</sup> Evidence is "relevant" if it has any tendency to make a fact more or less probable than it would be without the evidence, and the fact being proven or disproven is of consequence in determining the action.<sup>6</sup> The party seeking to have expert opinion testimony admitted into evidence bears the burden of demonstrating, by a preponderance of the evidence, that the expert's findings and conclusions are based on the scientific method and, therefore, are reliable.<sup>7</sup>

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<sup>3</sup> Kessler Report, at 159-61.

<sup>4</sup> Huss v. Gayden, 571 F.3d 442, 452 (5<sup>th</sup> Cir. 2009), *citing* Mathis v. Exxon Corp., 302 F.3d 448, 459 (5<sup>th</sup> Cir. 2002).

<sup>5</sup> F.R.E. 402.

<sup>6</sup> F.R.E. 401.

<sup>7</sup> Moore v. Ashland Chemical, Inc., 151 F.3d 269, 276 (5<sup>th</sup> Cir. 1998) (*en banc*).

The Federal Rules of Evidence require that a judge, faced with a proffer of expert scientific testimony, must begin by determining, pursuant to Rule 104(a), whether the expert is proposing to (i) testify to scientific knowledge (ii) that will assist the trier of fact to understand or determine fact in issue.<sup>8</sup> This will require a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue.<sup>9</sup> This requirement is found in Rule 702 of the Federal Rules of Evidence, which reads as follows in its entirety:

A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:

- (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
- (b) the testimony is based on sufficient facts or data;
- (c) the testimony is the product of reliable principles and methods; and
- (d) the expert has reliably applied the principles and methods to the facts of the case.

In the United States Supreme Court's landmark decision in Daubert v. Merrell Dow Pharmaceuticals, Inc., the Court acknowledged the existence of a federal court's gatekeeping role with regard to expert scientific opinion testimony, characterizing that role as one ensuring that such evidence meet the requirements of both reliability and relevance.<sup>10</sup> "Reliability" as discussed in Daubert refers to *evidentiary* reliability, *i.e.*, trustworthiness, rather than *scientific* reliability, which asks whether application of the principle produces consistent results, a

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<sup>8</sup> Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 592, 113 S.Ct. 2786, 2796, 125 L.Ed.2d 469 (1993).

<sup>9</sup> Id., 509 U.S. at 592-93; Moore, 151 F.3d at 276.

<sup>10</sup> Moore, 151 F.3d at 275.

distinction often blurred by Defendants' arguments. In a case involving scientific evidence, evidentiary reliability is based upon scientific validity, which asks whether the principle supports what it purports to show.<sup>11</sup>

The objective of this requirement is to make sure that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.<sup>12</sup> The Supreme Court identified several non-exclusive factors a court should consider in determining whether proffered scientific opinion testimony is sufficiently reliable to permit admission into the record.<sup>13</sup> Those factors are:

- whether the expert's theory can be or has been tested;
- whether the theory has been subject to peer review and publication;
- the known or potential rate of error of a technique or theory when applied;
- the existence and maintenance of standards and controls; and
- the degree to which the technique or theory has been generally accepted in the scientific community.<sup>14</sup>

Several years later, the Supreme Court clarified when it held the gatekeeping role applied to all types of expert opinion testimony, not just scientific evidence, and revisited the reliability analysis.<sup>15</sup> Moreover, the Supreme Court reiterated that a court must have considerable leeway in deciding, in a particular case, how to go about determining whether particular expert

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<sup>11</sup> Daubert, 509 U.S. at 590 n.9.

<sup>12</sup> Kumho Tire Company, Ltd. v. Carmichael, 526 U.S. 137, 152, 199 S.Ct. 1176, 143 L.Ed.2d 238 (1999). See also Brown v. Illinois Central Railroad Co., 705 F.3d 531, 535 (5<sup>th</sup> Cir. 2013).

<sup>13</sup> See discussion, 509 U.S. at 594-595.

<sup>14</sup> Moore, 151 F.3d at 275.

<sup>15</sup> Kumho Tire, 526 U.S. at 141-142.

testimony is reliable.<sup>16</sup> Therefore, the test of reliability is flexible and there is no necessary or exclusive list of factors that must exist in order for a particular opinion to be admissible.<sup>17</sup>

Daubert makes clear that the factors it mentions do not constitute a definitive checklist or test. Daubert adds that the gatekeeping inquiry must be tied to the facts of a particular case. We agree with the Solicitor General that the facts identified in Daubert may or may not be pertinent in assessing reliability, depending on the nature of the issue, the expert's particular expertise, and the subject of his testimony. The conclusion, in our view, is that we can neither rule out, nor rule in, for all cases and for all time the applicability of the factors mentioned in Daubert, nor can we now do so for subsets of cases categorized by category of expert or by kind of evidence. Too much depends upon the particular circumstances of the particular case at issue.<sup>18</sup>

In the Fifth Circuit, “[t]o determine whether proffered testimony is reliable, the trial court must make ‘a preliminary assessment of whether the reasoning or methodology underlying the testimony is . . . valid and of whether that reasoning or methodology properly can be applied to the facts in issue.’”<sup>19</sup> Further, “[t]o establish reliability under Daubert, an expert bears the burden of furnishing ‘some objective, independent validation of [his] methodology.’”<sup>20</sup> In doing so, “[t]he expert’s assurances that he has utilized generally accepted [principles] is insufficient.”<sup>21</sup>

In Brown the Fifth Circuit held that the trial court did not abuse its discretion where an expert testified that offered opinions were reliable merely upon and because of “education and experience” and did not engage in or rely upon a credible methodology, particularly in the face

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<sup>16</sup> Kumho Tire, 526 U.S. at 152.

<sup>17</sup> Id., at 141-142, 149.

<sup>18</sup> Id., at 150 (citations and quotation marks omitted).

<sup>19</sup> Brown v. Illinois Central Railroad Co., 705 F.3d 531, 535 (5th Cir. 2013) (quoting Daubert, 509 U.S. at 592-93).

<sup>20</sup> Brown, 705 F.3d at 536 (quoting Moore, 151 F.3d at 276).

<sup>21</sup> Id. (quoting Moore, 151 F.3d at 276).

of evidence in opposition to those opinions. Standing alone then, it is insufficient for an expert to base his or her opinion on education and experience alone, especially in the face of evidence to the contrary.

### ANALYSIS

Plaintiffs bear the ultimate burden on the admissibility of their proffered evidence, thus, this Court will first look to Plaintiffs' *prima facie* showing on each issue. If a *prima facie* showing is made, this Court will proceed to a consideration of the Defendants' specific challenges.

#### A. Opinions regarding Labels

As noted above, Dr. Kessler has reached the conclusion that, in his opinion, the warning labels used by Takeda "would have been inadequate." Dr. Kessler's opinion rests in part upon Dr. Kessler's opinion Takeda withheld two vital pieces of information from the FDA; these gaps in the FDA's knowledge, according to Dr. Kessler, led the FDA to require and approve labels that did not address bladder cancer. Dr. Kessler opines that with the requisite knowledge, the agency would have required the Actos® warning label to include a mention of the risk of bladder cancer. For purposes of the present argument, the Defendants do not contest either Dr. Kessler's analysis or his conclusions; their argument is limited to a legal one. Defendants argued the United States Supreme Court has held that state court "fraud-on-the-FDA" claims conflict with and, therefore, are impliedly pre-empted by, federal law. *See Buckman Company v. Plaintiffs' Legal Committee*.<sup>22</sup> The Defendants argue this preemption has the effect, in this case, of precluding Dr. Kessler from presenting *any* evidence that Takeda withheld information from the FDA. This Court disagrees. Plaintiffs are not pursuing a state law claim grounded in "fraud-on-

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<sup>22</sup> 531 U.S. 341, 348, 121 S.Ct. 1012, 1017, 148 L.Ed.3d 854 (2001) ("[W]e hold that the plaintiffs' state-law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by federal law.").

the-FDA,” to the contrary as prior rulings on motions for summary judgment, motions in limine, and the jurisprudence have made clear, what the FDA might or might not have done is not determinative of the legal issues before this Court. However, equally clear is the recognition that both the Defendants and Plaintiffs, in part, argue Takeda’s history with the FDA *as evidence of* what Takeda “*knew or should have known*” as to “all possible dangers” of Actos. Consequently, within this broad legal context evidence as to Takeda and its interaction with the FDA is – if otherwise admissible – relevant to the legal inquiry as to Plaintiffs’ tort claim grounded in “failure to adequately warn.”<sup>23</sup> Consequently, Defendants’ argument is misplaced and undercut by certain previous arguments made by Defendants which suggest Defendants intend to use the FDA as a “shield” in their defense of their conduct and knowledge.

Again, this Court notes, one must not lose sight of the actual claims made by Plaintiffs that will be pursued at trial. Plaintiffs will not be litigating a “fraud-on-the-FDA claim” as Defendants’ argument implies. Thus, Buckman does not, by its own terms, apply to this case and Defendants’ reliance upon it is misplaced. Moreover, additionally, even the Buckman Court acknowledged there are certain types of state law claims *based upon violations of the Federal Food, Drug, and Cosmetic Act (“FDCA”)*<sup>24</sup> that are not preempted, and distinguished the surviving claims by noting that pre-empted claims were based entirely *on alleged violations of* FDCA disclosure requirements;<sup>25</sup> that is not the factual scenario at play in the instant case. In

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<sup>23</sup> See: Martin v. Hacker, 83 N.Y.2d 1 (1993); Wolfruber v. Upjohn Company, 72 A.D.2d 59 (1979).

<sup>24</sup> See 52 Stat. 1040, as amended by 21 U.S.C. § 201, *et seq.* The Federal Food, Drug, and Cosmetic Act (“FDCA”) in this ruling is a statute and not to be confused with the United States Food and Drug Administration (“FDA”) an agency.

<sup>25</sup> “In the present case, however, the fraud claims exist solely by virtue of the FDCA disclosure requirements. Thus, although Medtronic can be read to allow certain state-law causes of actions that parallel federal safety requirements, it does not and cannot stand for the proposition that any violation of the FDCA will support a state-law claim.” Id., 531 U.S. at 352-3, 121 S.Ct. at 1020.

light of this distinction, Buckman does not govern, and, therefore, does not preclude any and all evidence of FDCA reporting violations, but in Buckman pre-empted *claims* based solely on those alleged violations. However, again this distinction, also, is not determinative of Defendants ill-fated challenge. Once again this Court notes that under the actual *tort* claim couched upon a “failure to adequately warn” of “all possible dangers” Takeda “knew or with exercise of reasonable care should have known,” evidence of the information provided to or allegedly withheld from the FDA about the risks, benefits, or dangers of Actos during the relevant time frame – i.e. from the creation of Actos until Mr. Allen stopped taking Actos,<sup>26</sup> is relevant to that broad inquiry. Again, whether such evidence in the manner presented might or might not be otherwise admissible is not the inquiry now before the Court and is better reserved until trial, however, the evidence is *relevant* to the issues inherent within the “failure to adequately warn” claim made by Plaintiffs and not precluded *by law* as Defendants argue. Thus, Defendants’ reliance on Buckman, is, in and of itself, misguided as to the actual legal question before the Court.

In their Reply, the Defendants argue the Fifth Circuit’s decision in Lofton v. McNeil Consumer & Specialty Pharmaceuticals,<sup>27</sup> interpreted Buckman and its preemption mandate so broadly that any mention of a failure to disclose information to the FDA is *legally* improper because of the *legal* application of preemption. However, this Court has read Lofton closely and notes several very important distinguishing factors. First, the Court was interpreting and applying a very specific *Texas statute* that *requires* a plaintiff *asserting a failure to warn claim*

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<sup>26</sup> *Baker v. St. Agnes Hosp.*, 70 A.D.2d 400,406 (N.Y. App. Div. 2d Dep’t 1979) (holding the continuing obligation of a drug manufacturer is twofold: (1) it must keep abreast of knowledge of its products as gained through research, adverse reaction reports, scientific literature and other available methods; and (2) it must take such steps as are reasonably necessary to bring that knowledge to the attention of the medical profession.).

<sup>27</sup> 672 F.3d 372 (5<sup>th</sup> Cir. 2012).

to prove *fraud-upon-the-FDA* in order to overcome a presumption of no liability, and *no such statute exists under New York law*. Rather, by contrast, New York law does not address, nor in any way require, proof of “fraud-upon-the FDA” in order to establish or recover under a failure to warn theory of products liability. Second, and perhaps more importantly, the district court in Lofton had made a finding, which appears to have been unchallenged on appeal, that *the FDA had already considered the same arguments the Loftons were asserting and had rejected those arguments*. As a result, the district court held that “section 82.007(b)(1) is preempted in *some* circumstances, including as here, *where Plaintiffs ask the court to reach the conclusion opposite of that reached by the FDA*, that Defendants did not withhold information or mislead it.”<sup>28</sup> Commenting later that the Loftons’ claims were “more factually and legally apposite” to the Buckman facts, the Fifth Circuit ultimately concluded as follows: “Because we conclude that § 82.007(b)(1) is a fraud-on-the-FDA provision analogous to the claim considered in Buckman, we hold that it is preempted by the FDCA unless the FDA itself finds fraud.”<sup>29</sup>

The Lofton Court did not expand the Buckman analysis in a manner as to establish a *legal finding* its determination *under the facts* of Lofton would apply across the board and as a matter of law, rather the Court found the *specific combination of facts and law with which it was presented* in Lofton had created, in effect, a replica of Buckman. No such combination of facts and law have been presented or exist in the matter at hand. Thus, to read Lofton as broadly as Defendants argue is unwarranted and ill-advised. Consequently, this Court disagrees with the Defendants’ broad interpretation of Lofton and finds it does not mandate the preemptive effect of Buckman under the facts of this case, where no “fraud-upon-the-FDA” claims are statutorily

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<sup>28</sup> Id. at 375. (emphasis added).

<sup>29</sup> Id. at 381.

mandated, or plead, and no related affirmative defenses will be litigated. Therefore, as Dr. Kessler's evidence and opinion are not *as a matter of law* precluded and clearly have relevance to issues which will be litigated – i.e. “what Takeda knew or should, with the exercise of reasonable care known” as to “all potential dangers” of Actos, within the relevant time frame,<sup>30</sup> as well as to Takeda's specific knowledge or credibility, the Defendants' argument Dr. Kessler should be wholly precluded from testifying, *as a legal issue*, is unpersuasive and, therefore, OVERRULED.

#### **B. The October 2005 Data Mining Results**

Defendants' challenge to Dr. Kessler is not, it would seem, limited solely to the legal challenge discussed above. Consequently, out of an abundance of caution, the Court will address the other challenges *implied* by Defendants' arguments made.

In October, 2005, Takeda conducted a “data mining” exercise where they ran a search of the FDA database for all adverse event reports for bladder cancer and found that bladder cancer was reported significantly more often with pioglitazone than with all other drugs compared (the data mining exercise yielded a result of “2.9”; as that number is unexplained by either party, this Court does not know its precise meaning, except that which can be inferred from what was argued, i.e. that bladder cancer events are reported with pioglitazone significantly more often than with other drugs). Dr. Kessler reviewed the Takeda data mining report and reached certain conclusions and now opines this information ought to have been reported to the FDA. The Defendants seek an order precluding him from offering such an opinion at trial, arguing Dr. Kessler lacks any “foundation or factual basis to assert that this was meaningful information that needed to be reported to FDA.”

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<sup>30</sup> See fn 23.

Dr. Kessler's analysis of this issue comprises eight (8) pages, and over thirty (30) paragraphs, of his Report, which:

- refers extensively to the Disproportionality Analysis conducted by Takeda as a result of the data mining exercise;
- discusses a request by the FDA issued in June, 2006 for new data regarding the bladder cancer risk;
- describes evidence suggesting that Takeda conducted a *second* data mining exercise, that did not include the same type of search that had yielded the 2.9 result in October, 2005; and
- concludes that "based on my experience as FDA Commissioner and thereafter as Chair of the compliance committees of FDA-regulated companies, in my opinion, Takeda's omission was highly concerning, improper and did not meet the standards of a reasonable and prudent pharmaceutical company."<sup>31</sup>

Dr. Kessler's opinion is based upon his review of information produced in this case by Takeda and his experience as the Commissioner of the FDA during the relevant time period. Moreover, Dr. Kessler has stated that the argued Disproportionality Analysis is the type of information that he saw, used, and based his decisions on while he served as Commissioner of the FDA and is the type of information he currently uses and evaluates when functioning as the Chair of certain compliance committees for other pharmaceutical companies regulated by the FDA. Based upon his knowledge, training, and experience with this type of information, he has reached certain conclusions, and opines that the Disproportionality Analysis contains meaningful information that should have been disclosed to the FDA. This conclusion and opinion do not lack a foundation, as discussed above. Defendants' possible *disagreement with* the foundation for the opinion given does not equate to a lack of foundation.

The Defendants make three more specific arguments as to why Dr. Kessler should not be allowed to testify on this point. First, they argue they were not obligated by regulation to

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<sup>31</sup> Kessler Report, at 21-28.

conduct the data mining exercise, therefore, they were under no obligation to report the results of the exercise. While it might be true that reporting the Disproportionality Analysis, alone, might not have been required,<sup>32</sup> the circumstances noted by Dr. Kessler are that whether required to or not, Takeda, in fact, did conduct the Disproportionality Analysis and, once conducted, Takeda was in possession of the information which he is of the opinion should have been provided. Furthermore, Dr. Kessler suggests the FDA specifically asked for any further data in the Defendants' possession in June, 2006, thus, making the information specifically within Takeda's reporting obligation. Consequently, Dr. Kessler's opinion this information *was* in Takeda's possession *and* as the FDA had requested any additional information, and the fact Takeda did not disclose it, is sufficiently grounded in fact as to be both relevant and admissible. The fact Takeda was under no obligation to conduct the analysis in the first instance is of no moment as to whether or not once information was known to them and additional information requested by FDA, they could ignore the information at their own peril. Again, the Court reminds all parties the *legal* issue before *this Court*, as to the tort of "failure to adequately warn," is, in part, what Takeda "knew or should have known," therefore, in theory, what Takeda reported or did not report to the FDA is, as Defendants argue, *legally* of no moment. However, *as a matter of evidence* relevant to prove up Takeda's conduct and knowledge – perhaps most particularly as to punitive damages, but, also, as to general liability – the information it had available and what use or lack thereof Takeda made of that information, is relevant. Furthermore, to the extent Defendants attempt to use the FDA review, approval and action or lack thereof as a shield, what information they provided to the FDA, *once additional information was known*, and *once*

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<sup>32</sup> See Defendants' Omnibus Exhibit G3, at 9-10.

*requested* is again, relevant. Defendants' argument on this point is both shortsighted and misplaced.

Second, the Defendants argue there was no obligation to report this new information to the FDA because the Disproportionality Analysis did not prove a causal link between pioglitazone and bladder cancer. Again, Defendants conflate two separate procedural possibilities and two separate evidentiary inquiries. Whether Takeda was or was not required to report the now known information *to the FDA* is of no real moment to whether an actual *causal* link existed. Rather, it is of moment as to what information Takeda knew or whether such information might or might not have suggested a "potential danger." For this threshold inquiry, it is sufficient that Takeda knew (or should have known with the exercise of reasonable care) of the argued information, for the information to relate to a "potential danger" for the information to be relevant. However, as to the punitive damage's claim, whether Takeda's *conduct* does or does not rise to the requisite standard of willfulness might well, also, embrace what, if anything, Takeda did with certain information it had, and thus, again, is relevant to that separate *legal* inquiry. Additionally, again, to the extent Takeda attempts to use evidence of FDA action or lack of action as a shield – as their arguments on previous motions indicate – what information Takeda provided or failed to provide to the FDA is clearly relevant. Consequently, again, Defendants' arguments are painted with too broad a brush or, perhaps, are viewed through a distorting, and myopic lens. The argument made by Defendants, it would seem, is based upon the premise that pharmaceutical companies regulated by the FDA are not required to produce data to the FDA until and *unless that data definitively proves causation* between a pharmaceutical and a side effect. However, Dr. Kessler notes the FDA regulations require

disclosure to patients of “evidence from human data that the drug *may* be carcinogenic. . .”<sup>33</sup> He further states that, as a former Commissioner of the FDA, he personally has used similar information in evaluating the safety of pharmaceuticals, and that FDA regulators use this type of information normally in the course of their work. Thus, even Defendants’ myopic argument is not persuasive in the face of the facts at hand. Again, whether the trier of fact will or will not agree with Dr. Kessler remains to be seen and Defendants are invited to engage in vigorous cross-examination, should they deem that appropriate, – however, Dr. Kessler will be allowed to voice his opinion on the matter at trial. This Court, also, finds Defendants’ argument suggesting the Defendants were legally permitted to withhold information suggesting an argued possible connection between pioglitazone and bladder cancer simply because the information was not definitive is so unpersuasive as to border on specious. To clarify, what Takeda was or was not bound to have reported to the FDA, might bear immediate relevance to the punitive damages claim, and, also, to rebuttal should Defendants attempt to use FDA action or inaction to defend their conduct and Dr. Kessler has presented a sufficient foundation to pass this threshold gatekeeper evaluation. Consequently, Defendants’ argument is unpersuasive, at best.

Third, the Defendants argue the information derived through the Disproportionality Analysis was meaningless.<sup>34</sup> This Court is in no position to determine what meaning, if any, to attribute to the information the Defendants obtained in October, 2005; that is for the experts to debate and the trier of fact to decide. Dr. Kessler (whose experience and training the Defendants

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<sup>33</sup> 21 C.F.R § 201.57(f)(5) (2005) (emphasis added).

<sup>34</sup> The Defendants point out the Disproportionality Analysis, standing alone is “no more than one set of numbers run through a computer.” (Memorandum, at 8) The Court notes this, likely, is an apt description for statistics and such complaint, likely, is not limited in any meaningful way to these particular statistics. It is how the statistics were created and for what purpose they are used that most often grants statistics their meaning and impact, if any. And while this Court might agree with Mark Twain’s oft quoted disdain of statistics, statistics, nonetheless, are firmly woven into the complex tapestries of our day to day lives and both Plaintiffs and Defendants’ legal and evidentiary arguments.

have made no effort to impeach) has declared his knowledge and experience mandate that he find the disputed information meaningful, and, of a nature such that it should have been reported to the FDA. This Court has no doubt the Defendants will produce an expert (in-house or otherwise) who says precisely the opposite. These conflicting viewpoints, however, are for the trier of fact and, thus, will be presented to the jury, whether through cross-examination or direct examination, and the jury will decide whom, if anyone, they believe on this point. The Defendants' challenge on this basis is again unpersuasive and overruled.

### **C. Opinions Regarding Misleading Promotion**

First, at this juncture, this Court must remind Defendants that Plaintiffs have plead, in addition to their "failure to adequately warn" claim, *torts* based upon "negligent marketing and negligent distribution. Consequently, the legal issues to which Dr. Kessler's opinion as to marketing might or might not be relevant is expanded beyond only the "failure to adequately warn" claim.

Dr. Kessler has two opinions concerning alleged misleading promotion of Actos® by the Defendants. First, Takeda argues Dr. Kessler's opinion as to Takeda's promotional activities since February, 2011 are irrelevant to the Plaintiffs' claims, as Mr. Allen's bladder cancer was diagnosed in January, 2011,<sup>35</sup> and Mr. Allen stopped taking Actos April of 2011. The Plaintiffs have not responded to this argument. This Court agrees that Dr. Kessler's opinion concerning the promotional activities associated with Actos® that occurred after January or April, 2011, likely, are not relevant and, therefore, likely, will be precluded, unless those opinions were to become relevant as to credibility, however, this Court cannot make that determination in a vacuum. Consequently, at this juncture, the Defendants' argument on this point is well taken and

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<sup>35</sup> Kessler Opinion, at 68-80; ¶¶ 204-231.

the objection sustained without prejudice to Plaintiffs to reurge should Defendants “open the door.”

Second, Dr. Kessler opines Takeda’s cardiovascular safety claims during its promotion of Actos® were misleading. The Defendants make four arguments Dr. Kessler’s opinion on this point should be precluded.

***Dr. Kessler’s Opinion is “contrary to law.”*** The Defendants make the same argument, based on the United States Supreme Court case of Buckman Company v. Plaintiffs’ Legal Committee and Lofton v. McNeil Consumer & Specialty Pharmaceuticals – that Dr. Kessler is not permitted to offer opinions based upon such alleged violations of the FDCA by the Defendants. The argument is overruled for the same reasons discussed above.

***Dr. Kessler’s Opinion Consists of Narrative Testimony.*** The objection that testimony is “narrative” is an objection as to form, foundation, or responsiveness, and must be presented at trial – *as no question is now before the Court to which objection can be made*. The objection is overruled at this time, without prejudice to the Defendants’ ability to re-urge their objection at the proper time depending upon the actual question asked. Again, this Court notes Defendants’ regrettable propensity to meld actual Daubert challenges with the more generic motion in limine challenges, as well as with objections which cannot be made until trial. Nonetheless, this Court has addressed the challenges now made and finds Defendants’ challenge on this point inappropriate at this juncture.

***Dr. Kessler’s Testimony contains “impermissible personal opinions.”*** The Defendants argue the Kessler Report “is an extensive summary of Takeda and FDA documents interspersed with conclusory personal opinions,”<sup>36</sup> citing ¶¶ 260 through 428, which are located on Pages 88

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<sup>36</sup> Memorandum, at 11.

through 152, some 67 pages of the Report. The Defendants have not identified the actual *opinions* they seek to have excluded and this Court will not go through the Report in an effort to divine Defendants' actual objection, nor should this Court.<sup>37</sup> As noted in Skotak v. Tenneco Resins, Inc.,<sup>38</sup> "Rule 56 does not impose upon the district court a duty to sift through the record in search of evidence to support a party's opposition to summary judgment." Suffice it to say, at this point this Court, generally, would agree with the Defendants that unsupported, unfounded expert opinions should not be presented at trial; if such an opinion is proffered, the Defendants will be free to object to a lack of foundation and this Court will rule at that time. Defendants' objection is denied as unsupported.

***Dr. Kessler's Qualifications.*** Finally, the Defendants argue Dr. Kessler stopped being Commissioner of the FDA in 1997 and, therefore, all of the current guidance on promotional activities was issued after he left the agency and, therefore, he should not be allowed to testify. As noted above, Dr. Kessler's actual qualifications have not been impeached or challenged by Defendants. Furthermore, this Court notes the evidence is, moreover, that Dr. Kessler has remained abreast of the FDA regulations and guidance not only by way of his present position held with multiple pharmaceutical companies, but, also, by way of his publications and industry involvement. Dr. Kessler published an article on the subject of drug promotion after he left the FDA; has given lectures on drug promotion since he left the FDA; and is, at present, involved in compliance issues associated with advertising and promotion in his capacity as chair of two

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<sup>37</sup> The only specific paragraph to which the Defendants have objected as containing "personal opinion" is ¶ 229, which has already been excluded because it deals with promotional activities that occurred after Mr. Allen's bladder cancer had already developed.

<sup>38</sup> 953 F.2d 909, 915-16 & n.7 (5<sup>th</sup> Cir.), cert. denied, 506 U.S. 832, 113 S.Ct. 98, 121 L.Ed.2d 59 (1992).

pharmaceutical company compliance committees. Consequently, Defendants' challenge on this basis as to Dr. Kessler's qualifications and expertise, *as an expert*, are wholly unpersuasive.

The Defendants, also, assert "Dr. Kessler may have had expertise on the FDA's regulation of advertising and promotion at one point, his experience is stale."<sup>39</sup> However, again, a matter better addressed at trial by way of vigorous cross-examination. Also, Defendants, once again, ignore the facts in play as discussed above. And the Court, once again, reminds Defendants, disagreement with is not synonymous with the absence of, and argument suggesting otherwise is unfortunate hyperbole and borders on inappropriate. The Defendants have not produced any evidence Dr. Kessler no longer knows or understands the regulatory control over promotion now exercised by the FDA, particularly in the face of evidence he has day to day responsibility for such regulatory control within his work, has written and lectured within the industry on these very issues and once headed the FDA. Again, the Defendants will be free to cross-examine Dr. Kessler at trial about his past and current understanding of the regulation of promotional activities by the FDA and pharmaceutical companies. Defendants' argument is unpersuasive and, thus, Defendants' objection is OVERRULED.

#### **D. Legal Opinions**

Defendants' challenge certain other opinions of Dr. Kessler as "legal opinion."

As noted above, Dr. Kessler is not only a physician; he is a lawyer, as well. The Defendants suggest that, in his Report, he has presented opinions that violate the strictures against lawyers (and other types of experts) testifying and usurping either the role of this Court or the role of the trier of fact.

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<sup>39</sup> Memorandum, at 13.

***Opinions as to Legal Standards.*** Beyond cavil, it is the role and duty of this Court to provide instructions to the jury on the law that they will be applying during the course of the trial and this is a duty this Court takes seriously and guards vigorously. This Court will cede that responsibility to no one, expert or lawyer. To the extent Dr. Kessler, or anyone else, were to seek to usurp this Court's role, all are on notice no such effort will be indulged and all parties are cautioned to fashion their questioning, argument and conduct with this truth in mind.

Specifically, the Defendants challenge certain statements by Dr. Kessler, asserting the statements constitute "impermissible legal standards" and argue Dr. Kessler should be precluded from proffering those statements at trial. However, this Court notes that the "legal standards" challenged and argued by the Defendants as objectionable are statements of Dr. Kessler's understanding of the meaning and application of certain statutes, regulations, and duties that were and are relevant to his ability to perform his past and present duties, both with the FDA and, at present, with his employing pharmaceutical companies. Dr. Kessler's report does not indicate an attempt by Dr. Kessler to instruct the jury as to *what the actual law applicable to the tort claims made by Plaintiffs* might be, rather, Dr. Kessler renders certain opinions as to Takeda's conduct and gives his understanding *as an expert* within that field, of the relevant regulations governing that conduct. If that conduct were not relevant to certain issues inherent in the tort claims made by the Plaintiffs, perhaps Defendants' argument would carry greater sway. However, that is not the case; Defendants, themselves, it would seem from arguments made in prior motions, argue their interaction with the FDA and the FDA's action, or lack thereof, is relevant to their defense in this case. To that extent, if not for other reasons as well, Dr. Kessler's opinions as the FDA Commissioner during the relevant time frame, are relevant and his understanding of the regulations which might apply are equally relevant to the issue raised by

Defendants. Again, Defendants' argument conflates and loses sight of the evidentiary and legal issues at hand. There is no question this Court will not allow Dr. Kessler – or any expert or attorney – to instruct the jury *as to what the applicable law in this case is*. However, again, *this case is not an administrative claim of FDA violation and whatever legal ramifications might statutorily flow from that violation* – rather, it is one based upon state law tort claims,<sup>40</sup> primary among them for this analysis, whether Takeda “failed to adequately warn” of “all potential dangers” Takeda “knew or should have known with the exercise of reasonable care” and whether Takeda’s conduct actually was or was not so egregious as to warrant punitive damages. Within this legal framework, again, Takeda’s interaction with the FDA bears relevance. Dr. Kessler, as the Commissioner of the FDA during the relevant time frame just preceding the FDA’s initial action on Actos, thus, posits certain opinions as to Takeda’s conduct vis-à-vis the FDA. Consequently, his understanding of the applicable rules and regulations is relevant to his state of mind and opinion made. Of course, Dr. Kessler is fully subject to vigorous cross-examination and Defendants are free to present contrary evidence and interpretation. However, Defendants’ argument on this point is unpersuasive. Again, the legal issue upon which liability might be predicated in this case is not governed by what the FDA regulations might or might not have been, but upon the declaration of the state of New York in its tort law.

Furthermore, to the extent Dr. Kessler’s opinions, as to the conduct of Takeda as to Actos *after* he left the FDA, might be otherwise admissible and might be relevant to a legal issue under *New York law*, they too would not be objectionable, on their face, as they do not run afoul of the tenet argued by Defendants. Again, defendants’ argument is misplaced. Dr. Kessler, by virtue of his experience as a former Commissioner of the FDA and as a Chair of compliance

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<sup>40</sup> This Court is not unaware of the contractual and quasi contractual claims, also, pled by Plaintiffs, however, those claims are not immediately relevant to the motion at hand.

committees in two companies that are currently regulated by the FDA, is sufficiently qualified to pass the gatekeeper's evaluation as to Daubert and the evidence contained within those opinions, on their face, are likely relevant *to the legal issues presented by the application of New York law of tort*. Defendants' argument that Dr. Kessler's testimony as to his understanding of the applicable rules and regulations governing interaction with the FDA suggests a flawed framing of the legal issue raised. An expert, it is undisputed, cannot instruct the jury as to applicable law, however, can rely upon his understanding of rules and regulations governing his industry when formulating his opinion. To argue otherwise illustrates a misunderstanding of the legal tenets at play.

Moreover, once again this Court reminds Defendants, the **legal question** before this Court is not whether there was a violation of FDA regulations. This is not an administrative proceeding asserting the violation of regulations, nor have the Plaintiffs alleged such a violation within the claims remaining before this Court. This portion of Defendants' argument is *evidentiary and not substantive* in nature, although Defendants conflate the two separate inquiries. Both the Plaintiffs and the Defendants argue the actions and inactions of the FDA are relevant to proof of their respective cases, with the Defendants wishing to use the FDA and its actions as a shield, while the Plaintiffs wish to use the FDA and its actions as a sword. Although it is likely this battle will rage throughout the trial as a matter of *evidence*, as a *matter of law* the Court will instruct the jury *as to the applicable New York law* which shall govern the actual claims made by the Plaintiffs. The two inquiries are, perhaps, interrelated but are quite distinct. Thus, again, Defendants' arguments are misplaced.

***Opinions as to Legal Conclusions.*** Defendants, also, argue the Kessler Report includes statements that opine as to certain of the ultimate issues that will be tried, *e.g.*, Takeda's actions

were improper under applicable New York law, and under the applicable New York law the Actos® label was inadequate. These conclusions (and others) represent the result of Dr. Kessler's application of the facts, as he believes them to be, to the law as he understands it and as will be instructed by the Court. He does not present these opinions as *legal* conclusions – i.e., violations as a matter of law – but his opinion as to how the *facts* will be applied to the applicable law - based upon the information he reviewed, the circumstances he considered, and his understanding of the application of those facts to the law as the Court will give to the jury by way of instruction. Depending upon how the actual questions and answers are framed, those questions might or might not be objectionable – a circumstance this Court cannot predict in a vacuum. This Court disagrees with the Defendants' broad characterization of Dr. Kessler's opinions and must await the legal context of actual questions and answers. Consequently, Defendants' argument, as made, is not persuasive.

However, this Court would note that Rule 704 of the Federal Rules of Evidence explicitly permits the submission of expert testimony that goes to the ultimate issue being tried. "An opinion is not objectionable just because it embraces an ultimate issue."<sup>41</sup> This Rule, adopted in 1972, abolished the historic "ultimate issue" rule in favor of one that **calls for a case-by-case analysis of each proffered opinion** that approaches the province of the trier of fact.

*The abolition of the ultimate issue rule does not lower the bar[] so as to admit all opinions. Under Rules 701 and 702, opinions must be helpful to the trier of fact, and Rule 403 provides for exclusion of evidence which wastes time. These provisions afford ample assurances against the admission of opinions which would merely tell the jury what result to reach, somewhat in the manner of the oath-helpers of an earlier day. They also stand ready to exclude opinions phrased in terms of inadequately explored legal criteria.*<sup>42</sup>

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<sup>41</sup> F.R.E. 704(a).

<sup>42</sup> F.R.E. 704, Advisory Committee Notes, 1972 Proposed Rules.

Consequently, as suggested by the comments, actual determination by a Court as to opinions which “embrace” the ultimate issue are no longer *presumed* objectionable. Rather the Court should *make a case-by-case analyses* of *each proffered opinion* and guard against opinions not helpful to the trier of fact or which waste time or merely tell the jury what result to reach. Necessary to this determination is, first, the context within the trial within which the opinion is to be presented, and second, knowledge of the actual question posed and/or answer given. For example, in a general negligence claim, a question which asks an expert if “the Defendant’s conduct was negligent” would likely be objectionable as that is the legal determination the jury is charged to make. However, a question which asks if “Defendant’s conduct created an unsafe condition in the expert’s opinion” likely would not, even though it goes to the ultimate issue, as the expert is merely giving his opinion as to the safety or lack thereof of Defendants’ conduct, within his given area of expertise. It would, therefore, remain for the attorneys to argue to the jury that the creation of an unsafe condition, under the applicable law, should constitute negligence. The distinction illustrated by the example now given is particularly significant given Dr. Kessler’s former position with the FDA and the authority that position might carry in the eyes of the jury.

Again, the *legal* issue is not whether or not the warning was deemed adequate or inadequate *as to FDA* regulations, rather, whether it was adequate or inadequate *as to applicable New York law*. What, if any *evidentiary* relevance the FDA determination might or might not have is likely to unfold only at trial. Dr. Kessler’s opinion as to the adequacy or inadequacy of the warning *as to New York law* is a different inquiry and not an inquiry this Court can engage in within a contextual vacuum. Rather, the inquiry is one which will likely be judged, upon

objection made at trial, within the context of the trial, itself, and the posture of the question asked.

Counsel, however, are cautioned that, although Dr. Kessler will be permitted to present his opinions at trial if the questions are framed prudently, he will not be permitted to invade the province of the jury or to simply offer his opinion in place of theirs. Consequently, Defendants' objection, at this juncture is **OVERRULED** without prejudice to their right to raise objections, if appropriate, at trial.

#### **E. Miscellaneous Objections**

In a section addressing a miscellany of objections, the Defendants assert Dr. Kessler uses narrative testimony, delivers personal opinions, uses "lawyer-like arguments,"<sup>43</sup> and engages in speculation. Although more often unsupported and poorly articulated, this Court will address those objections it can discern from Defendants' abbreviated argument.

*Narrative Testimony.* As was noted above, an objection to the "narrative" nature of testimony is an objection as to the form of a question or the foundation or responsiveness of a witness' answer, and is properly asserted at trial. Furthermore, it is not a proper objection to an *expert report*, that, itself, will not be placed into evidence, nor to a Daubert challenge.

Nor is it a proper objection to infer a report contains too much information as Defendants' argument suggests,<sup>44</sup> particularly when an expert is aware his report will be subject to detailed review by opposing counsel who are evaluating the sufficiency of his supporting data. Thus, Defendants' argument as to this issue borders on specious and is wholly without merit.

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<sup>43</sup> No actual argument addressing "lawyer-like" or other is included in the Memorandum.

<sup>44</sup> See Rule 26 (a)(2)(B) (an expert report *must contain*: (i) a complete statement of all opinions the witness will express *and the basis and reasons for them*; [and] (ii) *the facts or data considered by the witness in forming them*."") (emphasis added).

Dr. Kessler will be asked questions by Plaintiffs' counsel and Dr. Kessler will answer, whether those questions might or might not call for a narrative answer, remains to be seen and Dr. Kessler's report is not objectionable because of the amount of information it contains. Defendants' objection is OVERRULED.

***Personal Opinions and Conclusory Testimony.*** The Defendants object to four "examples of conclusory personal opinions." Each will be addressed in turn.

¶ 93. In Paragraph 93 of his report, Dr. Kessler concludes his discussion of Takeda's omission of the results of its data mining exercise (discussed more particularly above). Having discussed the matter for seven (7) pages and 27 paragraphs, Dr. Kessler states, in full:

Based on my experience as FDA Commissioner and thereafter as Chair of the compliance committees of FDA-regulated companies, in my opinion, Takeda's omission was highly concerning, improper and did not meet the standards of a reasonable and prudent pharmaceutical company.<sup>45</sup>

The opinion expressed in ¶ 93 is conclusive, in the sense that it presents Dr. Kessler's *conclusion* to this discussion, and supports his opinion on the subject of this rather extensive section of the report. Although it is the opinion of a person testifying *as an expert, here the expert, also, is testifying based upon his personal experience as the Commissioner of the FDA during the relevant time frame as to Actos*. However, neither basis of his testimony renders his testimony or opinion objectionable. It is without question a witness can testify as to his personal experience and actions if relevant to a legal issue before the Court. In this instance, if one is testifying, not as an expert, but as a lay witness as to one's own personal experience, of course and necessarily, that witness must testify from his or her personal experience, if relevant – in this instance it is that very personal experience – Dr. Kessler being Commissioner of the FDA during

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<sup>45</sup> Kessler Report, at 28.

the relevant time frame for Actos - which might or might not be relevant, depending upon the manner in which it is offered. It is equally without question *an expert* can testify *as to other than his own personal experience* and, if properly supported, render opinion on that beyond his personal experience – and Dr. Kessler grants such *expert opinion*. And it is equally without question – most particularly and usually found within the medical arena and, in particular, with treating physicians – often a witness – depending upon the circumstances – can do both. Although such a situation might present a challenge for counsel, it does not, in and of itself, necessarily, render the testimony, on its face, objectionable. Beyond this observation, this Court cannot address Defendants’ opaque argument, and Defendants’ objection is OVERRULED as wholly unsupported by either persuasive argument or evidence.

To the extent Defendants’ remaining cursory arguments challenge Dr. Kessler’s opinions in a more general context as “personal”, this Court notes Dr. Kessler clearly links his opinions to his experience as FDA Commissioner and as Chair of two compliance committees for FDA-regulated companies and the knowledge of the regulatory and industry landscape his training and experience provide. The Defendants provide this Court with no explanation for their suggestion that ¶ 93 contains “conclusory personal opinions,” nor do they explain their selective quotation of the paragraph.<sup>46</sup> Again, it is not for this Court to divine Defendants’ intent or legal challenge or argument. Their objections are OVERRULED.

¶ 146. In paragraph 146 of the Kessler Report, Dr. Kessler discusses certain scientific uncertainties about the PPAR activities triggered by Actos®, and opines the reasonable

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<sup>46</sup> In their Memorandum, the Defendants omit the first clause of the sentence in ¶ 93, in which Dr. Kessler links his opinion to his experiences, and start their quote with “Takeda’s omission was highly concerning. . .,” making it appear that the opinion is presented in a vacuum. Once again, this Court is compelled to caution Defendants as to presenting argument which ignores the facts surrounding that argument – disagreement with does not warrant exclusion of.

and prudent response to such uncertainties would have been to agree with the FDA's recommendation to include a sentence concerning bladder cancer in the package insert. Fully stated, Dr. Kessler's opinion is:

Furthermore, in my opinion, in the absence of having definitive information about these issues, a reasonable and prudent manufacturer, when confronted with this level of uncertainty regarding a serious hazard, would follow FDA's recommendations and issue the appropriate warnings.<sup>47</sup>

Once again, Dr. Kessler provides his opinion, as an expert, which reflects his conclusion about how a pharmaceutical company should respond to regulatory guidance when it cannot be certain what side effects are being caused by its drug, based upon his training, education and experience. As before, the opinion is based upon his experience as a regulator, together with his industry experience, scientific training, education, and amassed relevant knowledge. The Defendants, again, have not explained to this Court what might be unacceptable about an opinion so based – other than they might disagree with it, which is a matter for cross-examination and not one for the Daubert gatekeeper – nor, again, did they quote the entire relevant and challenged sentence, in their memorandum. Defendants' argument is unsupported, unpersuasive and, therefore, their objections are **OVERRULED**.

¶ 150. Paragraph 150 is directed to part of the same section of the Kessler Report as ¶ 146 (discussed above). In this paragraph, Dr. Kessler evaluates the response of Novo Nordisk when it received information, during clinical development of a diabetes medication, that the medication was triggering bladder tumors in animals:

Novo Nordisk's suspension of the clinical development of a PPAR agonist that demonstrated development of bladder tumors in animals is an

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<sup>47</sup> Kessler Report, at 44.

example of how a reasonable and prudent pharmaceutical manufacturer would respond to the finding of bladder tumors.<sup>48</sup>

Given Dr. Kessler's experience as a former Commissioner of the FDA and his current experience as Chair of compliance committees of two FDA-regulated companies, it is unclear to this Court how this opinion is either "conclusory" or "personal" in an improper way. Furthermore, although possibly not necessarily relevant to the issue of general liability, as what other companies might or might not have done under any given circumstances might or might not be relevant to that inquiry, it cannot be said, at this juncture, to be wholly irrelevant to the judgment the jury will be asked to make as to whether or not punitive damages should apply – that remains a judgment better left to the context of the trial.

As before, the Defendants have not supported, explained, or persuasively argued their objection to the inadmissibility of Dr. Kessler's opinion. The objection is **OVERRULED**.

¶ 364. Paragraph 364 presents Dr. Kessler's opinion found at the end of his discussion of Takeda's efforts to promote Actos® from September 2005 through February 2007, which Dr. Kessler opines is based upon a selective reading of information obtained through the PROactive study:

In my opinion, Takeda's improper promotion of ACTOS' cardiovascular efficacy is of further concern because the lack of any Warning of the risk of bladder cancer to counter the inadequately supported safety claims of reduced cardiovascular events.<sup>49</sup>

As before, Dr. Kessler's experience as a former Commissioner of the FDA and his current experience as Chair of compliance committees of two FDA-regulated companies appear to provide ample foundation for his opinion. It is unclear to this Court how this opinion is either

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<sup>48</sup> Kessler Report, at 45.

<sup>49</sup> Kessler Report, at 132.

“conclusory” or “personal” in an improper way and this Court notes and adopts its discussion given above. As before, the Defendants have not explained their argument for the inadmissibility of this opinion and their objection is not supported by fact or persuasive argument and, therefore, the objection is OVERRULED.

*Speculation as to Knowledge, Motive and Intent.* The last of the miscellaneous objections in this section allege Dr. Kessler “offers many impermissible opinions regarding knowledge, intent, and state of mind, including the following” six examples. The Defendants then list six “examples of knowledge, motive, and intent testimony” without providing explanation as to what might make them impermissible. This Court has reviewed all six statements – including the last, in which the Defendants complain Dr. Kessler implies something about Takeda’s intent<sup>50</sup> – and finds that each is supported within his report by sometimes-lengthy discussion of the data, information, and he notes the sources upon which these statements are founded. The evidence at trial might very well show that some, all, or none of Dr. Kessler’s opinions and statements are sound and the jury might grant those opinions no weight – but again, that is the purview of the trier of fact – not the gatekeeper when, as here, the expert’s Report reveals that none are, on their face, speculative in nature, but are, on their face, based upon his review of reams of documents and information. Furthermore, this Court cannot make this determination in a vacuum. Whether the actual question asked, or opinion given is framed so as to attempt to “read Takeda’s mind” and thus, would be objectionable, is a matter this Court cannot know as this juncture, and within a vacuum. The objection as to speculation as presented,

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<sup>50</sup> In fact, again, contrary to Defendants’ argument, the facts illustrate Dr. Kessler doesn’t *imply* anything, rather *states his opinion*: “*In my opinion, based on my FDA experience, Takeda failed to look for and uncover the increased risk of bladder cancer with ACTOS and, instead, explained away the risks.*” Kessler Report, at 84, ¶ 242.

however, is OVERRULED without prejudice to the Defendants' ability to re-urge their objection at trial, as appropriate, and to engage in vigorous cross-examination.

**F. Expertise-Related Challenges**

In their final group of challenges, the Defendants urge this Court to preclude Dr. Kessler from testifying as to four areas of "hard science."

*Testimony as to Meta-Analysis Conducted by Dr. David Madigan.* According to Dr. Kessler, Dr. David Madigan<sup>51</sup> conducted a meta-analysis of the PROactive study results. Dr. Kessler relied on the results of Dr. Madigan's analysis to reach his, Dr. Kessler's, opinion that "based on the above analyses and on my FDA experience, there was a statistically significant increase in bladder cancer among patients taking ACTOS compared to placebo/comparators and reported to the [sic] Takeda as of January 2004."<sup>52</sup> The Defendants do not challenge Dr. Kessler's epidemiological conclusions, *rather, question his ability to discuss the fact that he relied on Dr. Madigan's meta-analysis in reaching his conclusions.* It is without question, the facts and data upon which an expert may base his or her opinion(s) are admissible on that basis alone; Dr. Kessler needn't be a statistician to rely on statistics and analyses conducted by a statistician, particularly within this factual context when statistical analysis is, in part, one of the foundations upon which epidemiological analyses and conclusions are based and when epidemiological analyses and conclusions have, within the motion practice, been shown to be at the center of the scientific debate at hand. The Defendants' argument as presented, is, again, unsupported and unpersuasive and, therefore, the objection is OVERRULED.

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<sup>51</sup> Dr. Madigan is a statistician whose testimony will be presented at trial by the Plaintiffs.

<sup>52</sup> Kessler Report, at 39, ¶ 125.

*Statistical Significance of Results from Data Mining Exercise.* In another challenge to the admissibility of Dr. Kessler's opinion addressing Takeda's failure to provide to the FDA its own Disproportionality Analysis created in October, 2005, the Defendants suggest Dr. Kessler has never conducted data mining, himself, and, therefore, he is unqualified to understand and opine about the results of Takeda's data mining exercise. However, the Report clearly demonstrates Dr. Kessler has substantial experience reading, interpreting, and using data mining results, and this Court has been presented no evidence or persuasive argument suggesting that Dr. Kessler intends to opine *as the statistician or as a veteran data miner*. Again, Defendants are directed to cross-examination and Defendants' argument, as made herein, is unsupported and unpersuasive and, therefore, the objection is OVERRULED.

**PPARs.** The Defendants acknowledge Dr. Kessler is a physician with a "general understanding of what PPARs are." This admission, itself, establishes Defendants do not challenge Dr. Kessler's prima facie qualifications to discuss PPAR agonists. However, the Defendants, nonetheless, object to his ability to present any testimony as to PPAR agonist drugs because he has not conducted testing on PPAR agonists, has never published any paper on the subject of PPAR agonists, and, therefore, is unqualified to opine on the subject. Again, as an expert in his field, Dr. Kessler need not, himself, have conducted certain testing if he is relying on otherwise reliable testing conducted by experts in their respective fields and when Defendants, themselves, admit Dr. Kessler possesses "a general understanding of what PPARs are."

The Kessler Report reveals Dr. Kessler to have an understanding of both PPARs and PPAR agonists. This understanding was derived from his medical training and his experience at the FDA. Moreover, the Report reveals that, on its face, the educational information contained

in the Report appears well-researched and founded upon information Dr. Kessler seems to have gathered for the purpose of developing opinions in this case. Dr. Kessler is not presented as an expert on PPAR and PPAR agonists, and, on its face, for purpose of this Court's gatekeeping role, Dr. Kessler appears to have the expertise *to conduct the necessary research* to obtain relevant and reliable information and to possess the basic information necessary to provide the jury general education of the areas within the context of the opinions he renders. Of course, and as always, vigorous cross-examination might prove otherwise, however, and again, that is for the trial and the role of cross-examination. This Court finds Defendants' objections to Dr. Kessler's qualifications required to present the information in his Report concerning both PPARs and PPAR agonists to be wholly unpersuasive.

***Diabetes and its Treatment.*** Finally, the Defendants agree the Kessler Report does *not* contain any opinions about diabetes and its treatment, and yet Defendants seek an order of this Court precluding him from proffering opinions about diabetes and its treatment. In the absence of any reason to believe Dr. Kessler intends to violate the bounds of his Report, this Court will not reach out and issue an order precluding him from doing so. Both Dr. Kessler and the Plaintiffs' counsel are aware of the limitations imposed by Rule 26 of the Federal Rules of Civil Procedure and this Court's scheduling order. This Court trusts that they will – as will Defendants' counsel and their experts – abide by those limitations. Defendants' argument on this point is, on its face, specious in light of Defendants' admitted recognition Dr. Kessler's report does not contain the opinion they ask this Court to preclude. Defendants' objection is **OVERRULED.**

### EVIDENTIARY HEARING

The Defendants requested this Court agree to hear live testimony from the experts prior to ruling on the instant motion; this Court carefully considered the Defendants' request. The decision of how to go about ruling on the instant motion is squarely within this Court's discretion.

The trial court must have the same kind of latitude in deciding *how* to test an expert's reliability, and to decide whether and when special briefing or other proceedings are needed to investigate reliability, as it enjoys when it decides whether or not that expert's relevant testimony is reliable. Our opinion in Joiner makes clear that a court of appeals is to apply an abuse-of-discretion standard when it reviews a trial court's decision to admit or exclude expert testimony. That standard applies as much to the trial court's decisions about how to determine reliability as to its ultimate conclusion. Otherwise, the trial judge would lack the discretionary authority needed both to avoid unnecessary "reliability" proceedings in ordinary cases where the liability of an expert's methods is properly taken for granted, and to require appropriate proceedings in the less usual or more complex cases where cause for questioning the expert's reliability arises. Indeed, the Rules seek to avoid unjustifiable expense and delay as part of their search for truth and the just determination of proceedings.<sup>53</sup>

This Court reviewed the extensive briefing provided by both parties, as well as the large number of exhibits, including expert reports, depositions, and other documents, and concluded the nature of the challenges presented and the arguments made did not illustrate a need for live testimony. Live testimony would not be likely to contribute to any greater understanding of the nature of the dispute than can be and has been found in a careful reading and analysis of the briefs and accompanying evidence and documentation. The request for an opportunity to present live testimony in an evidentiary hearing is DENIED.

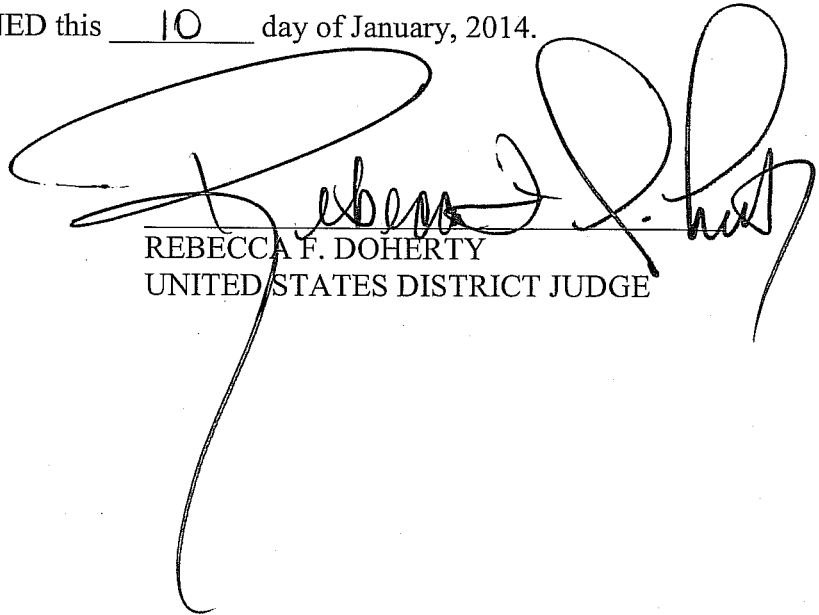
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<sup>53</sup> Kumho Tire, 526 U.S. at 152-53 (emphasis in original) (citations and quotations omitted).

**CONCLUSION**

For the foregoing reasons, the Defendants' Motion to Exclude Testimony of Plaintiffs' Expert, David Kessler, M.D., shall be DENIED IN PART and GRANTED IN PART.

THUS DONE AND SIGNED this 10 day of January, 2014.



REBECCA F. DOHERTY  
UNITED STATES DISTRICT JUDGE